0			2002/11/1 9 11:15	USPAT; US-PGPUB; EPO; 2002, JPO; DERWENT 9 11	6 same 13		L14 0	BRS	14
0			2002/11/1 9 11:15	USPAT; US-PGPUB; EPO; 2002 JPO; DERWENT 9 11	39709 control\$4 same 7 (transmission or pain)	39709. 7	L13	BRS	13
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FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT

11:18:01 ON 19 NOV 2002

- L1 881 S CLOSTRIDIAL NEUROTOXIN
- L2 19773 S (BOTULINUM TOXIN) OR (BOTULINUM NEUROTOXIN)
- L3 20134 S L1 OR L2
- L4 145857 S LECTIN
- L5 9696 S L4 (P) (GALACTOSE OR GALACTOSYL OR

ACETYLGALACTOSAMINE) (P)

- L6 1 S L3 (P) L5
- L7 48 S L3 (P) L4
- L8 26 DUPLICATE REMOVE L7 (22 DUPLICATES REMOVED)
- L9 15675 S L4 (P) (GALACTOSE OR GALACTOSYL OR

ACETYLGALACTOSAMINE)

- L10 1 S L9 (P) L3
- L11 6 S L8 (P) (CONJUGATE OR COVALENT?)
- L12 5 S L11 NOT L6
- L13 88211 S LIGHT CHAIN
- L14 433 S TRANSLOCATION DOMAIN
- L15 4 S L3 (P) L13 (P) L14
- L16 0 S L15 (P) L4

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FILE 'HOME' ENTERED AT 11:17:28 ON 19 NOV 2002 => file medline caplus biosis embase scisearch agricola COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 0.21 0.21 FILE 'MEDLINE' ENTERED AT 11:18:01 ON 19 NOV 2002 FILE 'CAPLUS' ENTERED AT 11:18:01 ON 19 NOV 2002 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS) FILE 'BIOSIS' ENTERED AT 11:18:01 ON 19 NOV 2002 COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC. (R) FILE 'EMBASE' ENTERED AT 11:18:01 ON 19 NOV 2002 COPYRIGHT (C) 2002 Elsevier Science B.V. All rights reserved. FILE 'SCISEARCH' ENTERED AT 11:18:01 ON 19 NOV 2002 COPYRIGHT (C) 2002 Institute for Scientific Information (ISI) (R) FILE 'AGRICOLA' ENTERED AT 11:18:01 ON 19 NOV 2002 => s clostridial neurotoxin L1881 CLOSTRIDIAL NEUROTOXIN => s (botulinum toxin) or (botulinum neurotoxin) L219773 (BOTULINUM TOXIN) OR (BOTULINUM NEUROTOXIN) => s l1 or l2 20134 L1 OR L2 => s lectin 145857 LECTIN => s 14 (p) (galactose or galactosyl or acetylgalactosamine) (p) bind? 9696 L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE) (P) BIND? => s 13 (p) 151 . 1 L3 (P) L5 => d 16 1 ibib abs ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1999:249106 CAPLUS DOCUMENT NUMBER: 130:276767 TITLE: Conjugates of ***galactose*** - ***binding*** ***lectins*** and ***clostridial*** ***neurotoxins*** as analgesics INVENTOR(S): Duggan, Michael John; Chaddock, John Andrew PATENT ASSIGNEE(S): The Speywood Laboratory Limited, UK; Microbiological Research Authority SOURCE: PCT Int. Appl., 50 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9917806 Al 19990415 WO 1998-GB3001 19981007

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,

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              CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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                                            AU 1998-93574
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     ZA 9809138
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                             19990527
                                            ZA 1998-9138
                                                             19981007
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                       A1
                             20000503
                                            EP 1998-946571
                                                             19981007
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, FI
      JP 2001518522
                        T2
                             20011016
                                            JP 2000-514674
                                                             19981007
PRIORITY APPLN. INFO.:
                                         GB 1997-21189
                                                        A 19971008
                                         WO 1998-GB3001
                                                          W 19981007
AB
     A class of novel agents that are able to modify nociceptive afferent
     function is provided. The agents may inhibit the release of
     neurotransmitters from discrete populations of neurons and thereby reduce
     or preferably prevent the transmission of afferent pain signals from
     peripheral to central pain fibers. They comprise a ***galactose***
        ***binding***
                         ***lectin***
                                         linked to a deriv. of a
       ***clostridial***
                              ***neurotoxin*** . The deriv. of the
       ***clostridial***
                             ***neurotoxin***
                                                comprises the L-chain, or a
     fragment thereof, which includes the active proteolytic enzyme domain of
     the light (L) chain, linked to a mol. or domain with membrane-
     translocating activity. The agents may be used in or as pharmaceuticals
     for the treatment of pain, particularly chronic pain.
REFERENCE COUNT:
                         6
                               THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
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L2
          19773 S (BOTULINUM TOXIN) OR (BOTULINUM NEUROTOXIN)
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          20134 S L1 OR L2
L4
         145857 S LECTIN
1.5
           9696 S L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE) (P)
              1 S L3 (P) L5
L6
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            48 L3 (P) L4
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         15675 L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE)
=> s 19 (p) 13
L10
             1 L9 (P) L3
=> s 18 (p) (conjugate or covalent?)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L75 (P) '
T.11
             6 L8 (P) (CONJUGATE OR COVALENT?)
=> s ll1 not l6
L12
             5 L11 NOT L6
=> d 112 1-5 ibib abs
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L12 ANSWER 1 OF 5

ACCESSION NUMBER:

DOCUMENT NUMBER:

MEDLINE

MEDLINE

PubMed ID: 12105193

2002470902

22218001

TITLE: Inhibition release of neurotransmitters from rat dorsal root gangli by a novel ***conjugate***

Clostridium ***botulinum*** ***toxin*** A endopeptidase fragment and Erythrina cristagalli

lectin

AUTHOR: Duggan Michael J; Quinn Conrad P; Chaddock John A; Purkiss John R; Alexander Frances C G; Doward Sarah; Fooks Sarah J;

Friis Lorna M; Hall Yper H J; Kirby Elizabeth R; Leeds Nicola; Moulsdale Hilary J; Dickenson Anthony; Green G Mark; Rahman Wahida; Suzuki Rie; Shone Clifford C; Foster

eith A

CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down,

Salisbury, Wiltshire SP4 OJG, United Kingdom.

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Sep 20) 277 (38)

34846-52.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200210

ENTRY DATE: Entered STN: 20020917

Last Updated on STN: 20021026 Entered Medline: 20021024

AΒ ***Clostridial*** ***neurotoxins*** potently and specifically inhibit neurotransmitter release in defined cell types. Here we report that a catalytically active derivative (termed LH(N)/A) of the type A neurotoxin from Clostridium botulinum has been coupled to a ***lectin*** obtained from Erythrina cristagalli to form a novel ***conjugate*** This ***conjugate*** exhibits an in vitro selectivity for nociceptive afferents compared with the anatomically adjacent spinal neurons, as assessed using in vitro primary neuronal culture systems to measure inhibition of release of neurotransmitters. Chemical ***conjugates*** prepared between E. cristagalli ***lectin*** and either natively sourced LH(N)/A or recombinant LH(N)/A purified from Escherichia coli are assessed, and equivalence of the recombinant material are demonstrated. Furthermore, the dependence of inhibition of neurotransmitter release on the cleavage of SNAP-25 is demonstrated through the use of an endopeptidase-deficient LH(N)/A ***conjugate*** variant. The duration

of action of inhibition of neurotransmitter released by the

conjugate in vitro is assessed and is comparable with that
observed with Clostridium ***botulinum*** ***neurotoxin***.

Finally, in vivo electrophysiology shows that these in vitro actions have
biological relevance in that sensory transmission from nociceptive
afferents through the spinal cord is significantly attenuated. These data
demonstrate that the potent endopeptidase activity of ***clostridial***

neurotoxins can be selectively retargeted to cells of interest and that inhibition of release of neurotransmitters from a neuronal population of therapeutic relevance to the treatment of pain can be achieved.

L12 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:228744 CAPLUS

DOCUMENT NUMBER: 134:247267

TITLE: Clostridial neurotoxin targeted conjugates for

inhibition of secretion from non-neuronal cells Foster, Keith Alan; Chaddock, John Andrew; Purkiss,

John Robert; Quinn, Conrad Padraig

PATENT ASSIGNEE(S): Microbiological Research Authority, UK

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

INVENTOR(S):

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021213	A2	20010329	WO 2000-GB3669	20000925
WO 2001021213	A3	20020711		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

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LU, LV, MA, MD, MG MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
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             SD, SE, SG, SI, SR
                                                                   , VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                       A2 20020904
                                          EP 2000-962721
                                                           20000925
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.:
                                        GB 1999-22554
                                                         A 19990923
                                                         W 20000925
                                        WO 2000-GB3669
AB
     A method of treatment of disease by inhibition of cellular secretory
     processes is provided. The method has particular application in the
     treatment of diseases dependent on the exocytotic activity of endocrine
     cells, exocrine cells, inflammatory cells, cells of the immune system,
     cells of the cardiovascular system, and bone cells. Agents and compns.
     therefor, as well as methods for manufg. these agents and compns., are
     provided. In a preferred embodiment a clostridial neurotoxin,
     substantially devoid of holotoxin binding affinity for neuronal cells of
     the presynaptic muscular junction, is assocd. with a targeting moiety.
     The targeting moiety is selected such that the clostridial toxin conjugate
     so formed may be directed to a non-neuronal target cell to which the
     conjugate may bind. Following binding, a neurotoxin component of the
     conjugate, which is capable of inhibition of cellular secretion, passes
     into the cytosol of the target cell by cellular internalization
     mechanisms. Thereafter, inhibition of secretion from the target cell is
     effected.
L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                         2000:706999 CAPLUS
DOCUMENT NUMBER:
                         133:261538
TITLE:
                         Use of a lectin or lectin conjugate for modulation of
                         C-fiber activity, and therapeutic use thereof
INVENTOR(S):
                         Foster, Keith Alan; Chaddock, John Andrew; Quinn,
                         Conrad Padraiq
PATENT ASSIGNEE(S):
                         Microbiological Research Authority, UK
SOURCE:
                         PCT Int. Appl., 62 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                    KIND DATE
                                         APPLICATION NO. DATE
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     WO 2000057897 A1 20001005
                                         WO 2000-GB1247 20000331
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
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            ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
            LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
            SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
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         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
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                      A1 20020102
                                         EP 2000-914295
                                                            20000331
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            IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.:
                                        GB 1999-7429
                                                         A 19990331
                                                       W 20000331
                                        WO 2000-GB1247
```

AB The invention relates to the treatment of pain and to compds. that modulate C-fiber activity. In particular, the invention relates to the ***lectin*** in the manuf. of a medicament for modulation of C-fiber neuron activity, and to ***lectin*** ***conjugates*** The ***lectin*** ***conjugates*** comprise a ***lectin*** coupled to a peptide or protein, wherein the peptide or protein is substantially free of ***Clostridial*** ***neurotoxin*** enzyme activity. The invention also concerns methods for manufg. the ***conjugates*** . The compds. and compns. described have particular application in the treatment of diseases of which C-fiber activity is a component. Such diseases include pain, inflammation, psoriasis and other C-fiber related conditions.

L12 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2000:144760 CAPLUS

DOCUMENT NUMBER:

132:175838

TITLE:

Compounds inhibiting exocytosis in mucus-secreting

cells or neurotransmitter release from neurons that control or direct mucus secretion for treatment of

mucus hypersecretion

INVENTOR (S):

Quinn, Conrad Padraig; Foster, Keith Alan; Chaddock,

John Andrew

PATENT ASSIGNEE(S):

Microbiological Research Authority, UK

SOURCE:

PCT Int. Appl., 30 pp.

DOCUMENT TYPE:

CODEN: PIXXD2

Patent

LANGUAGE:

FAMILY ACC. NUM. COUNT:

English

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010598	A2	20000302	WO 1999-GB2806	19990825
WO 2000010598	A 3	20000615		
£7 7.77 C/3	TD 110			

W: AU, CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

CA 2341429 AA 20000302 CA 1999-2341429 19990825 AU 9955250 A1 20000314 AU 1999-55250 19990825 EP 1107794 A2 20010620 EP 1999-941754 19990825

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2002523377 T2 20020730 PRIORITY APPLN. INFO.:

GB 1998-18548 A 19980825 WO 1999-GB2806 W 19990825

19990825

JP 2000-565918

AB A method of treating mucus hypersecretion, the causative factor in chronic obstructive pulmonary disease (COPD), asthma, and other clin. conditions involving COPD, comprises administering a compd. that inhibits exocytosis in mucus secreting cells or neurons that control or direct mucus secretion. Also described is a compd., for use in the treatment of hypersecretion of mucus, which inhibits mucus secretion by inhibiting mucus secretion by mucus secreting cells, and/or inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion.

L12 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: DOCUMENT NUMBER:

2002:520037 BIOSIS PREV200200520037

TITLE:

Characterisation of a novel ***conjugate*** A endopeptidase

fragment and E. cristagalli ***lectin***

AUTHOR (S):

Ling, R. J. (1); Fretwell, R.; Alexander, F.; Fooks, S.; Leeds, N.; Jameson, K.; Hall, Y.; Kirby, E.; Chaddock, J.;

Shone, C.

CORPORATE SOURCE:

(1) Centre for Applied Microbiology and Research, Porton

Down, Salisbury, Wiltshire, SP4 0JG UK

SOURCE:

Naunyn-Schmiedeberg's Archives of Pharmacology, (June, 2002) Vol. 365, No. Supplement 2, pp. R28. print. Meeting Info.: International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins

Hannover, Germany June 08-12, 2002

ISSN: 0028-1298.

DOCUMENT TYPE: LANGUAGE:

Conference English

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 L4
          145857 S LECTIN
            9696 S L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE) (P)
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               1 S L3 (P) L5
L7
              48 S L3 (P) L4
              26 DUPLICATE REMOVE L7 (22 DUPLICATES REMOVED)
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              1 S L9 (P) L3
               6 S L8 (P) (CONJUGATE OR COVALENT?)
L11
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               5 S L11 NOT L6
=> s light chain
         88211 LIGHT CHAIN
=> s translocation domain
L14
           433 TRANSLOCATION DOMAIN
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              4 L3 (P) L13 (P) L14
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          20134 S L1 OR L2
L4
         145857 S LECTIN
L5
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L7
             48 S L3 (P) L4
L8
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              6 S L8 (P) (CONJUGATE OR COVALENT?)
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              5 S L11 NOT L6
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          88211 S LIGHT CHAIN
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